

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1-52. (Cancelled)

53. (Currently Amended) A system comprising:

(i) an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome, and

(ii) a cell having a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, wherein

(a) if the adenoviral vector is deficient in one or more essential gene functions of the E2A region, the cellular genome comprises a nucleic acid sequence that complements for the deficiency in the E2A region that is operably linked to an inducible promoter or a repressible promoter, and

(b) if the adenoviral vector is deficient in one or more essential gene functions of the E4 region, the cellular genome comprises a nucleic acid sequence that complements for the deficiency in the E4 region that is operably linked to an inducible promoter or a repressible promoter,

and wherein there is no overlap between the cellular genome and the adenoviral genome that mediates a recombination event between the cellular genome and the adenoviral genome resulting in a replication-competent adenoviral vector.

54. (Previously Presented) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

55. (Previously Presented) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome, and the cell has a cellular genome that

complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E4 region of the adenoviral genome.

56. (Previously Presented) The system of claim 55, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

57. (Previously Presented) The system of claim 55, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

58. (Previously Presented) The system of claim 57, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

59. (Previously Presented) The system of claim 57, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

60. (Previously Presented) The system of claim 59, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

61.-62. (Cancelled)

63. (Currently Amended) A method of propagating an adenoviral vector, which method comprises

(a) providing an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome,

(b) providing a cell comprising a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or

both of the E2A region and the E4 region of the adenoviral genome, wherein there is no overlap between the cellular genome and the adenoviral genome that mediates a recombination event between the cellular genome and the adenoviral genome resulting in a replication competent adenoviral vector, and wherein

- (1) if the adenoviral vector is deficient in one or more essential gene functions of the E2A region, the cellular genome comprises a nucleic acid sequence that complements for the deficiency in the E2A region that is operably linked to an inducible promoter or a repressible promoter, and
 - (2) if the adenoviral vector is deficient in one or more essential gene functions of the E4 region, the cellular genome comprises a nucleic acid sequence that complements for the deficiency in the E4 region that is operably linked to an inducible promoter or a repressible promoter, and
- (c) propagating the adenoviral vector in the cell.

64. (Previously Presented) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

65. (Previously Presented) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in the E4 region of the adenoviral genome.

66. (Previously Presented) The method of claim 65, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

67. (Previously Presented) The method of claim 65, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

68. (Previously Presented) The method of claim 67, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1

region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

69. (Previously Presented) The method of claim 67, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

70. (Previously Presented) The method of claim 69, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

71.-72. (Cancelled)

73. (Previously Presented) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E2A region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E2A region of the adenoviral genome.

74. (Previously Presented) The system of claim 73, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

75. (Previously Presented) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome.

76. (Previously Presented) The system of claim 75, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1

region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

77. (Previously Presented) The system of claim 75, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

78. (Previously Presented) The system of claim 77, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

79. (Previously Presented) The system of claim 77, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

80. (Previously Presented) The system of claim 79, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

81. (Previously Presented) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E2A region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E2A region of the adenoviral genome.

82. (Previously Presented) The method of claim 81, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

83. (Previously Presented) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome and the cell has

a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of both the E2A region and the E4 region of the adenoviral genome.

84. (Previously Presented) The method of claim 83, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

85. (Previously Presented) The method of claim 83, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

86. (Previously Presented) The method of claim 85, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

87. (Previously Presented) The method of claim 85, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

88. (Previously Presented) The method of claim 87, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

89.-90. (Cancelled)

91. (Previously Presented) The system of claim 53, wherein the adenoviral genome is a human adenoviral genome.

92. (Previously Presented) The system of claim 91, wherein the adenoviral genome is an Ad5 adenoviral genome.

93. (Previously Presented) The system of claim 55, wherein the adenoviral genome is a human adenoviral genome.

94. (Previously Presented) The system of claim 93, wherein the adenoviral genome is an Ad5 adenoviral genome.

95. (Previously Presented) The method of claim 63, wherein the adenoviral genome is a human adenoviral genome.

96. (Previously Presented) The method of claim 95, wherein the adenoviral genome is an Ad5 adenoviral genome.

97. (Previously Presented) The method of claim 65, wherein the adenoviral genome is a human adenoviral genome.

98. (Previously Presented) The method of claim 97, wherein the adenoviral genome is an Ad5 adenoviral genome.